



to find promising metabolic engineering strategies by utilizing OptFlux (Rocha *et al.* 2010). OptFlux is an extensive metabolic modelling platform that offers state of the art strain simulations and evolutionary algorithms, enabling the identification of beneficial genetic modifications and environmental conditions, as well as flux analysis throughout a metabolic network. This will allow the identification of an optimal metabolic system for conduction of alternative terpenoid production pathways. Finally, information about transcriptional regulation of metabolic genes in *Saccharomyces cerevisiae* will be used to implement a model of Boolean rules, providing an additional regulatory layer to enable improved control on flux distribution. This combined metabolic and regulatory model will be used to design *Saccharomyces cerevisiae* cell factories capable of efficient terpenoid production.

Rocha I, Maia P, Evangelista P, Vilaça P, Soares S, Pinto JP, Nielsen J, Patil KR, Ferreira EC & Rocha M. OptFlux: an open-source software platform for in silico metabolic engineering. BMC Systems Biology. 2010, 4:45

## Development of Novel Genome-Scale Reconstruction Strategies for Production of Terpenoids in *Saccharomyces Cerevisiae*.

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Terpenoid compounds are widely used as biofuels, food additives, fragrances and pharmaceuticals. However, production of these compounds requires high amounts of resources and applicable production pathways are limited. The native production pathway for terpenoid compounds in *Saccharomyces cerevisiae* is the mevalonate pathway, which leads from acetyl-CoA to isopentenyl diphosphate, the basic molecule of which terpenoid compounds are composed of. In recent years, several optimization approaches for terpenoid production via the mevalonate pathway have been published. These optimizations include overexpression of participating enzymes by gene amplification or promoter exchange, alteration of enzymes, abundant provision of substrates and co-factors, and limitation of competing pathways to guide fluxes towards the product of interest. Despite these advances, terpenoid production remains cost-intensive, and few regulation mechanisms have been exploited so far. To tackle these problems, this work aims to utilize metabolic modelling strategies to identify alternative pathways, implement them in *Saccharomyces cerevisiae* models, and include a model on transcriptional regulation of metabolic genes. First, enumeration algorithms are applied on databases of known metabolic reactions to find all possible alternative pathways connecting the strain metabolites to different key terpenoid compounds which serve as precursors to multiple other terpenoid compounds. These alternative pathways are then introduced into a Yeast 7 model which will be optimized